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| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/806,580 | REIMANN ET AL. | |
| | Examiner | Art Unit | |
| | Myron G. Hill | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *38- 53, 55, 56, 59, 60, and 64- 66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38- 53, 55, 56, 59, 60, and 64- 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

This action is in response to paper filed 15 January 2004.

This action is on claims 38- 53, 55, 56, 59, 60, and 64- 66.

### *Rejections Withdrawn*

### *Claim Rejections - 35 USC § 112*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 38- 53, 55, 56, 59, 60, and 64- 66 are under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Applicant points to locations in the specification that define the terms. The terms are defined such that the metes and bounds of the limitations are clear.

The rejection of claims 38- 53, 55, 56, 59, 60, and 64- 66 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments and the clarity of the definitions as stated above make this rejection moot.

The rejection of claims 38- 53, 55, 56, 59, 60, and 64- 66 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to unstable proteins that stable when expressed as a fusion with a modified T antigen that precipitates with a HSP73.

Applicant's arguments are persuasive.

***New Rejections***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58 and 64- 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for intro recognition of peptide epitopes, does not reasonably provide enablement for inducing immune responses and vaccines against all unstable proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are drawn to vaccines.

There are not vaccines for all viral antigens. In Example 6 (page 32, last paragraph) Applicant states N-terminal and internal fragments are hard to express and cites the example of SIV. While many types of vaccination have been shown successful with HBV, retroviruses, in particular HIV, have not had the same successes. The specification does not sufficiently support the claimed vaccines. The term "vaccine" by definition implies any preparation intended for active immunological prophylaxis; e.g., preparations of killed microbes of virulent strains or living microbes of attenuated (variant or mutant) strains; or microbial, fungal, plant, protozoal, or metazoan derivatives or products. Although just about any protein when inoculated can cause an immune reaction, the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined. Prophylaxis is defined as the prevention of disease or of a process that can lead to disease. This is achieved by use of an antigenic (immunogenic) agent to actively stimulate the immunological mechanism, or the administration of chemicals or drugs to members of a community to reduce the number of carriers of a

disease and to prevent others contracting the disease. The specification describes the elicitation of an immunoglobulin response to a Nef-Tat fusion protein in mice. There is insufficient evidence that such a study would correlate with *in vivo* efficacy in humans. It is well known in the art that retroviral therapies, especially HIV therapies, are refractory to anti-viral therapies. The obstacles to developing a successful therapy of HIV are well documented in the literature. These obstacles include 1) the extensive genomic diversity and mutation rate associated with the HIV retrovirus, particularly with the respect to the gene encoding the envelope protein. 2) The fact that the mode of viral transmission includes both virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert manner, as well as via free virus transmission. 3) The establishment of a latent viral infection. 4) The ability of the virus to evade the immune responses in the central nervous system due to the blood-brain barrier. 5) The complexity and variation of the pathology of HIV infection in different individuals. 6) The inability of a natural infection to one strain of HIV to protect an individual from being infected with another strain of HIV. These obstacles establish that the contemporary knowledge in the art would not allow one of skill in the art to use the claimed vaccine to treat and/or prevent HIV infection without undue experimentation.

Furthermore, it is well known in the art that individuals infected with HIV produce neutralizing antibodies to the virus, yet these antibodies are not protective and do not prevent the infection from progressing to its lethal conclusion.

Applicants have not provided any convincing evidence that their claimed vaccine is indeed useful as a therapeutic or preventative for HIV infection or other viral diseases

and have not provided sufficient guidance in to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 38- 53, 55, 56, 59, 60, and 64- 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schirmbeck *et al.* (Eur. J. of Immuno., 1997, from IDS) and Fu *et al.*

This invention is drawn to a polynucleotide encoding a fusion protein which is stable in as cell

Schirmbeck *et al.* teaches a nucleic acid encoding a T-antigen with a C-terminal deletion, that this T-antigen complexes with a HSP73, and is stable in cells for at least 6 hours (page 2022, column 1, middle paragraph).

Schirmbeck *et al.* do not teach a peptide that is unstable in a cell.

Fu *et al.* teach that nucleic acid sequences encoding peptides (CTL epitopes) can be inserted in the T-antigen coding sequence in at least one location and be expressed and recognized in a cell (page Figures 1 and 2).

One of ordinary skill in the art at the time of invention would have known that the half-life of short peptides would be short because they would be quickly degraded. One of ordinary skill in the art at the time of invention would have known the usefulness of expressing exogenous CTL epitopes because they are useful for generating specific immune responses as shown by Fu *et al.* in vitro (Figure 4) and that this can used in vivo to induce long term T-cell responses for antibody production (page 6869, column 2, last paragraph). One of ordinary skill in the art at the time of invention would have been motivated to add exogenous peptide epitopes to the sequence of Schirmbeck *et al.* because it would provide a stable method of presenting peptides that are not stable by themselves. Because of the immune properties of expressed CTL peptides and other antigenic peptides, the product when used can induce an immune response.

Thus, it would be prima facie obvious to add the epitopes to the stable T-antigen mutants of Schirmbeck *et al.* with the expectation of success because Fu *et al.* shows that the unstable peptides can be expressed as a T- antigen fusion peptide.

## ***Conclusion***

No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 571-272-0901. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Myron G. Hill
Patent Examiner
July 12, 2004

JAMES HOUSEL
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7/12/04